

IN THE CLAIMS:

1. (Original) A method of treating a patient suffering from accumulation of a metabolite within macrophages, said method comprising treating the patient with a macrophage depleting amount of a bisphosphonate compound, such that apoptosis of macrophages is induced and the metabolite is released into circulation so that it may be eliminated from the patient.
2. (Original) The method of claim 1, wherein the bisphosphonate compound is clodronate.
3. (Original) The method of claim 1, wherein the patient is suffering from Gaucher's disease, and the metabolite is GL1.
4. (Original) The method of claim 3, further comprising administering to the patient a composition of purified recombinant glucocerebrosidase.
5. (Original) The method of claim 1, wherein the patient is suffering from Niemann-Pick disease, and the metabolite is sphingomyelin.
6. (Original) The method of claim 5, further comprising administering to the patient a composition of purified recombinant acid sphingomyelinase.
7. (Currently amended) A method of treating a patient suffering from accumulation of a metabolite within macrophages, said method comprising treating the patient with a macrophage depleting amount of a bisphosphonate compound, such that apoptosis of macrophages is induced, and administering to the patient a gene therapy vector encoding a compound which is able to break down the accumulated metabolite.
8. (Original) The method of claim 7, wherein the patient is suffering from Gaucher's disease, and the gene therapy vector encodes glucocerebrosidase.
9. (Original) The method of claim 8, further comprising administering to the patient a composition of purified recombinant glucocerebrosidase.
10. (Original) The method of claim 7, wherein the patient is suffering from Niemann-Pick disease, and the gene therapy vector encodes acid sphingomyelinase.
11. (Original) The method of claim 10, further comprising administering to the patient a composition of purified recombinant acid sphingomyelinase.
12. (Original) The method of claim 7, wherein the patient is suffering from Fabry's disease, and the gene therapy vector encodes alpha-galactosidase A.

13. (Original) The method of claim 12, further comprising administering to the patient a composition of purified recombinant alpha-galactosidase.

14. (Original) The method of claim 7, wherein the patient is suffering from Pompe disease, and the gene therapy vector encodes alpha-glucosidase.

15. (Original) The method of claim 14, further comprising administering to the patient a composition of purified recombinant alpha glucosidase.

16. (Original) The method of claim 7, wherein the patient is suffering from Hurler 's Disease (MPS-I), and the gene therapy vector encodes alpha-L iduronidase.

17. (Original) The method of claim 16, further comprising administering to the patient a composition of purified recombinant alpha-L iduronidase.

18. (Currently amended) The method of claim 7, further comprising administration of a macrophage depleting or macrophage inhibiting compound selected from the group consisting of doxorubicin doxicirubin, gamma globulin, and neutral polymers.

19. (New) A method comprising the steps of:

- a) first administering an effective amount of a macrophage inhibiting agent such that the endocytic or phagocytic activity of the macrophages is inhibited; and then
- b) administering an effective amount of a gene therapy vector.

20. (New) A method according to claim 7, wherein macrophage depleting agent is a bisphosphonate selected from the group consisting of clodronate, alendronate, pamidronate, zolendronate, etidronate, ibandronate, olpadronate, risedronate, medronate, neridronate, tiludronate, and incadronate.

21. (New) A method according to claim 19, wherein macrophage inhibiting agent is selected from the group consisting of doxorubicin, gamma globulin, heavy metal salts, and molecules capable of blocking Fc receptors.

22. (New) The method of claim 19, wherein the patient is suffering from Gaucher's disease, and the gene therapy vector encodes glucocerebrosidase.

23. (New) The method of claim 22, further comprising administering to the patient a composition of purified recombinant glucocerebrosidase.

24. (New) The method of claim 19, wherein the patient is suffering from Niemann-Pick disease, and the gene therapy vector encodes acid sphingomyelinase
25. (New) The method of claim 24, further comprising administering to the patient a composition of purified recombinant acid sphingomyelinase.
26. (New) The method of claim 19, wherein the patient is suffering from Fabry's disease, and the gene therapy vector encodes alpha-galactosidase A.
27. (New) The method of claim 26, further comprising administering to the patient a composition of purified recombinant alpha-galactosidase.
28. (New) The method of claim 19, wherein the patient is suffering from Pompe disease, and the gene therapy vector encodes alpha-glucosidase.
29. (New) The method of claim 28, further comprising administering to the patient a composition of purified recombinant alpha glucosidase.
30. (New) The method of claim 19, wherein the patient is suffering from Hurler 's Disease (MPS-I), and the gene therapy vector encodes alpha-L iduronidase.
31. (New) The method of claim 30, further comprising administering to the patient a composition of purified recombinant alpha-L iduronidase.
32. (New) A method according to claims 7 or 19, wherein the gene therapy vector is selected from the group comprising adenoviral vectors, adeno-associated viral vectors, or DNA vectors.